

- 6 -

M is a detection marker indirectly linked to A to form a detection marker-analyte binding partner complex;

- 5 A is an analyte binding partner which is specifically recognised by the analyte. In some embodiments, A is an antigen bearing an epitope which is specifically recognised by an antibody to be detected. In some embodiments, A is either bound to X_1 , A is expressed as part of X_1 or occurs naturally as part of X_1 ;
- 10 X_1 and X_2 comprise bridge binding partners which form a bridging complex between the detection marker (M) and the analyte binding partner (A) and are bound by (+) which is a reversible non-covalent bond;
- 15 X_1 comprises a first bridge binding partner which is a particle, dimer, multimer, chimera or fusion protein comprising a portion which binds to X_2 and another portion which binds to or comprises the analyte binding partner (A) and wherein the adjacent (—) is a covalent or non-covalent bond between the first bridge binding partner and the analyte binding partner (A);
- 20 By particle is meant a viral particle or a viral like particle. In some embodiments, X_1 comprises a recombinant viral-like particle comprising a proteinaceous analyte binding partner. In some embodiments, the viral like particle is derived from an avian hepadnavirus and the antigen is expressed as a part of the L polypeptide.
- 25 X_2 comprises a second bridge binding partner which is bound, fused or otherwise directly or indirectly connected to the detectable marker (M) and wherein the adjacent (—) is a covalent or non-covalent bond. In some embodiments, X_2 is connected to the detectable marker using one or more pairs of binding molecules such as antibody-antibody biotin-streptavidin or biotin-anti-biotin antibody pairs.

- 37 -

CLAIMS:

1. A method for detecting an antibody in a sample, the method comprising contacting the sample with components of a detection marker-antibody complex for a time and under conditions such that the detection marker is connected indirectly to an antigen recognised by the antibody to be detected by a bridging complex which preserves or enhances the availability of binding sites on the antigen for the antibody, and wherein the bridging complex comprises proteins X_1 and X_2 and wherein X_1 comprises a viral particle or viral-like particle, a dimeric or multimeric protein, or a chimeric or fusion protein which comprises an epitope recognised by the antibody to be detected and also binds reversibly to X_2 , wherein X_2 is bound by X_1 and is also bound, fused or otherwise connected to the detection marker, and detecting the detection marker to indicate the presence of the antibody in the sample.
2. The method of claim 1, wherein components of the detection marker-antigen complex are stored or used separately or together.
3. The method of claim 2, wherein the detection marker- X_2 component and the X_1 -antigen component are stored separately.
4. The method of claim 1, wherein the antibody is one or more of an IgM, IgE, IgA and IgG antibody.
5. The method of claim 1, wherein X_2 comprises an antibody, protein binding molecule, nucleic acid binding molecule, carbohydrate binding molecule or lipid binding molecule.
6. The method of any one of claims 1 to 5, wherein X_1 is a viral particle comprising multiple copies of a binding site recognised by the antibody to be detected and wherein X_2 comprises an antibody which binds to the binding site, and wherein X_2

- 38 -

is contacted with X_1 such that only one or a few of the binding sites are bound leaving further binding sites on the virus particle to react with the antibody to be detected.

7. The method of claim 6, wherein X_1 is an isolated or recombinant hepatitis viral particle.
8. The method of claim 7, wherein the hepatitis viral particle is a hepatitis A viral particle.
9. The method of claim 7, wherein the hepatitis viral particle is a hepatitis B viral particle.
10. The method of claim 7, wherein the hepatitis viral particle is a hepatitis C viral particle.
11. The method of claim 7, wherein the hepatitis viral particle is a hepatitis E viral particle.
12. The method of claim 6, wherein X_1 and X_2 are stored separately and form a complex during performance of the method.
13. The method of claim 6, wherein the detection marker comprises one or more of a mass tag, dye, colloidal or magnetic-particle, enzyme, radioactive molecule, chemiluminophore, fluorphore, phosphorescent molecule, luminescent molecules such as firefly luciferase, metal and metalloid, metal complexes, microparticles, nucleic acids, phosphors, dielectric, paramagnetic and/or phosphorescent particles, photoproteins, quantum dots, radioisotopes, redox complexes, substrates, viruses or other equivalent molecule.

- 39 -

14. The method of claim 1, wherein X_1 is an avian hepadnavirus virus-like particle (VLP).
15. The method of claim 14, wherein X_1 comprises multiple copies of a binding site recognised by the antibody to be detected and wherein X_2 comprises an antibody which binds to the binding site, and wherein X_2 is contacted with X_1 such that only one or a few of the binding sites are bound leaving further binding sites on the VLP to react with the antibody to be detected.
16. The method of claim 14, wherein X_2 binds to a binding site on the VLP not recognised by the antibody to be detected.
17. The method of claim 14, wherein the VLP is a recombinant duck hepadnavirus-like particle and X_2 is a monoclonal antibody determined by the S or L antigen of duck Hepadnavirus.
18. The method of claim 14, wherein the detection marker comprises one or more of a mass tag, dye, colloidal or magnetic-particle, enzyme, radioactive molecule, chemiluminophore, flurophore, phosphorescent molecule, luminescent molecules such as firefly luciferase, metal and metalloid, metal complexes, microparticles, nucleic acids, phosphors, dielectric, paramagnetic and/or phosphorescent particles, photoproteins, quantum dots, radioisotopes, redox complexes, substrates, viruses or other equivalent molecule.
19. The method of any one of claims 1 to 5, wherein X_1 is a dimeric or multimeric protein comprising at least two binding sites recognised by the antibody to be detected and wherein X_2 comprises an antibody which binds to the binding site, and wherein X_2 is contacted with X_1 such that only one or a few of the binding sites are bound leaving further binding sites on the dimer or multimer to react with the antibody to be detected.

- 40 -

20. The method of claim 19, wherein X_1 is dimeric ORF2.1 antigen of hepatitis E virus
21. The method of claim 19, wherein the detection marker comprises one or more of a mass tag, dye, colloidal or magnetic-particle, enzyme, radioactive molecule, chemiluminophore, flurophore, phosphorescent molecule, luminescent molecules such as firefly luciferase, metal and metalloid, metal complexes, microparticles, nucleic acids, phosphors, dielectric, paramagnetic and/or phosphorescent particles, photoproteins, quantum dots, radioisotopes, redox complexes, substrates, viruses or other equivalent molecule.
22. The method of any one of claims 1 to 4, wherein X_1 is a fusion or chimeric protein comprising the antigen and a second binding partner which binds reversibly to X_2 , wherein X_2 comprises an antibody or a protein binding molecule or carbohydrate binding molecule or lipid binding molecule or nucleic acid binding molecule bound by the second binding partner.
23. The method of claim 22, wherein the second binding partner is a carbohydrate and X_2 comprises a carbohydrate binding protein.
24. The method of claim 22, wherein the second binding partner is a protein and X_2 comprises a protein binding protein.
25. The method of claim 22, wherein the detection marker is a mass tag, dye, colloidal particle, enzyme, radioactive molecule, chemiluminophore, flurophore, phosphorescent molecule, luminescent molecules such as firefly luciferase, metal and metalloid, metal complexes, microparticles, nucleic acids, phosphors, dielectric, paramagnetic and/or phosphorescent particles, photoproteins, quantum dots, radioisotopes, redox complexes, substrates, viruses or other equivalent molecule.

- 41 -

26. The method of any one of claims 13, 18, 21 or 25, wherein the detection marker is a colloidal particle, such as colloidal gold, silver or selenium.
27. The method of claim 1, wherein the antibody is immobilised to a solid support prior to detection.
28. The method of any one of claims 1 to 27 when used for detecting one or a plurality of specific antibodies in a sample.
29. The method of any one of claims 1 to 28 when used for detecting one or a plurality of specific antibodies to hepatitis such as hepatitis A and/or B and/or C and/or E in a sample.
30. The method of claim 1, wherein the method is a chromatographic or immunochromatographic method.
31. A kit for detecting a specific antibody in a sample, in compartmental form comprising a portion to receive the sample and a portion to receive components of a detection marker-antigen complex, wherein the antigen comprises an epitope recognised by the antibody to be detected, if present in the sample, and wherein the detection marker is connected indirectly to the antigen by a bridging complex which preserves or enhances the availability of epitopes on the antigen for the antibody and detection thereof relative to a control, and wherein the bridging complex comprises bridge binding partners X_1 and X_2 wherein X_1 comprises a viral particle or virus-like particle, a dimeric or multimeric protein, or a chimeric or fusion protein which comprises an epitope recognised by the antibody to be detected and binds reversibly to X_2 , wherein X_2 comprises an antibody or an protein binding molecule which is bound by X_1 and which is bound, fused or otherwise connected to the detection marker.

- 42 -

32. The kit of claim 31, wherein components of the detection marker-antigen complex are stored or used separately or together.
33. The kit of claim 31, wherein the detection marker- X_2 component and the X_1 -antigen component are stored separately.
34. The kit of claim 31, wherein the specific antibody in the sample is one or more of an IgM, IgE, IgA and IgG antibody.
35. The kit of claim 31, wherein X_2 comprises an antibody, protein binding molecule, nucleic acid binding molecule, carbohydrate binding molecule or lipid binding molecule.
36. The kit of any one of claims 31 to 35, wherein X_1 is a viral particle comprising multiple copies of a binding site recognised by the antibody to be detected and wherein X_2 comprises an antibody which binds to the binding site, and wherein X_2 is contacted with X_1 such that only one or a few of the binding sites are bound leaving further binding sites on the virus particle to react with the antibody to be detected.
37. The kit of claim 36, wherein X_1 is an isolated or recombinant hepatitis viral particle.
38. The kit of claim 37, wherein the hepatitis viral particle is a hepatitis A viral particle.
39. The kit of claim 37, wherein the hepatitis viral particle is a hepatitis B viral particle.
40. The kit of claim 37, wherein the hepatitis viral particle is a hepatitis C viral particle.
41. The kit of claim 37, wherein the hepatitis viral particle is a hepatitis E viral particle.

- 43 -

42. The kit of claim 36, wherein X_1 and X_2 are stored separately and form a complex during use of the kit.
43. The kit of claim 36, wherein the detection marker comprises one or more of a mass tag, dye, colloidal or magnetic-particle, enzyme, radioactive molecule, chemiluminophore, fluorphore, phosphorescent molecule, luminescent molecules such as firefly luciferase, metal and metalloid, metal complexes, microparticles, nucleic acids, phosphors, dielectric, paramagnetic and/or phosphorescent particles, photoproteins, quantum dots, radioisotopes, redox complexes, substrates, viruses or other equivalent molecule.
44. The kit of claim 31, wherein X_1 is an avian hepadnavirus virus-like particle (VLP).
45. The kit of claim 44, wherein X_1 comprises multiple copies of a binding site recognised by the antibody to be detected and wherein X_2 comprises an antibody which binds to the binding site, and wherein X_2 is contacted with X_1 such that only one or a few of the binding sites are bound leaving further binding sites on the VLP to react with the antibody to be detected.
46. The kit of claim 44, wherein X_2 binds to a binding site on the VLP not recognised by the antibody to be detected.
47. The kit of claim 44, wherein the VLP is a recombinant duck hepadnavirus-like particle and X_2 is a monoclonal antibody determined by the S or L antigen of duck Hepadnavirus.
48. The kit of claim 44, wherein the detection marker comprises one or more of a mass tag, dye, colloidal or magnetic-particle, enzyme, radioactive molecule, chemiluminophore, fluorphore, phosphorescent molecule, luminescent molecules such as firefly luciferase, metal and metalloid, metal complexes, microparticles, nucleic acids, phosphors, dielectric, paramagnetic and/or phosphorescent particles,

- 44 -

photoproteins, quantum dots, radioisotopes, redox complexes, substrates, viruses or other equivalent molecule.

49. The kit of any one of claims 31 to 35, wherein X_1 is a dimeric or multimeric protein comprising at least two binding sites recognised by the antibody to be detected and wherein X_2 comprises an antibody which binds to the binding site, and wherein X_2 is contacted with X_1 such that only one or a few of the binding sites are bound leaving further binding sites on the dimer or multimer to react with the antibody to be detected.
50. The kit of claim 49, wherein X_1 is dimeric ORF2.1 antigen of hepatitis E virus.
51. The kit of claim 49, wherein the detection marker comprises one or more of a mass tag, dye, colloidal or magnetic-particle, enzyme, radioactive molecule, chemiluminophore, fluorophore, phosphorescent molecule, luminescent molecules such as firefly luciferase, metal and metalloid, metal complexes, microparticles, nucleic acids, phosphors, dielectric, paramagnetic and/or phosphorescent particles, photoproteins, quantum dots, radioisotopes, redox complexes, substrates, viruses or other equivalent molecule.
52. The kit of any one of claims 31 to 34, wherein X_1 is a fusion or chimeric protein comprising the antigen and a second binding partner which binds reversibly to X_2 , wherein X_2 comprises an antibody or a protein binding molecule or carbohydrate binding molecule or lipid binding molecule or nucleic acid binding molecule bound by the second binding partner.
53. The kit of claim 52, wherein the second binding partner is a carbohydrate and X_2 comprises a carbohydrate binding protein.
54. The kit of claim 52, wherein the second binding partner is a protein and X_2 comprises a protein binding protein.

- 45 -

55. The kit of claim 52, wherein the detection marker is a mass tag, dye, colloidal particle, enzyme, radioactive molecule, chemiluminophore, fluorphore, phosphorescent molecule, luminescent molecules such as firefly luciferase, metal and metalloid, metal complexes, microparticles, nucleic acids, phosphors, dielectric, paramagnetic and/or phosphorescent particles, photoproteins, quantum dots, radioisotopes, redox complexes, substrates, viruses or other equivalent molecule.
56. The kit of any one of claims 43, 48, 51 or 55, wherein the detection marker is a colloidal particle, such as colloidal gold, silver or selenium.
57. The kit of claim 31, wherein the antibody is immobilised to a solid support prior to detection.
58. The kit of any one of claims 31 to 57 when used for detecting one or a plurality of specific antibodies in a sample.
59. The kit of any one of claims 31 to 58 when used for detecting one or a plurality of specific antibodies to hepatitis such as hepatitis A and/or B and/or C and/or E in a sample.
60. The kit of claim 31, wherein the kit is a chromatographic or immunochromatographic kit.